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Radical Arylalkoxycarbonylation of 2-Isocyanobiphenyl with Carbazates: Dual C−C Bond Formation toward Phenanthridine-6-carboxylates

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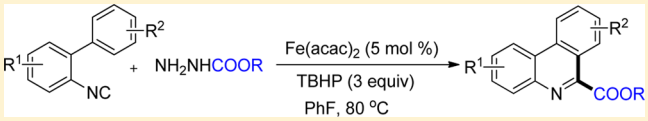
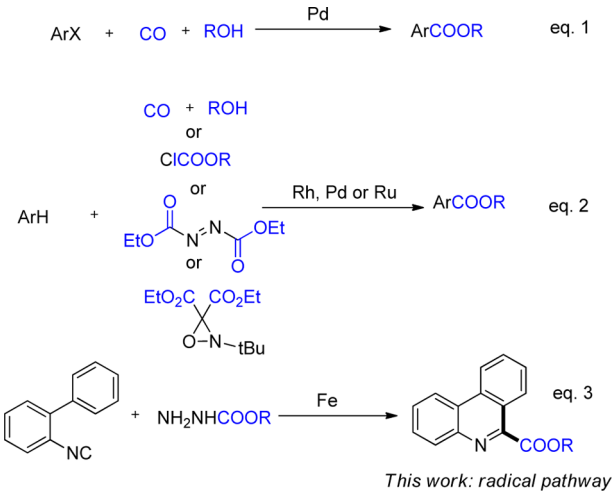
Supporting Information

ABSTRACT: A sequential oxidative radical alkoxycarbonylation and aromatization of 2-isocyanobiphenyl with carbazates was developed to furnish phenanthridine-6-carboxylates. Various functional groups such as methoxy, chloro, fluoro, trifluoromethoxy, and trifluoromethyl groups were tolerated well under the reaction conditions. The sequential radical addition−cyclization strategy represents a practical route to access phenanthridine-6-carboxylates.



Carbonylation reactions are powerful tools for the construction of C−C bonds in synthetic chemistry.[1] Among these reactions, alkoxycarbonylation is highly valuable since it enables the direct introduction of an ester moiety into organic compounds.[2] Generally, CO and alcohols are applied as the source of the ester group in alkoxycarbonylation of ArX (Scheme 1, eq 1). Recently, great efforts have been dedicated to developing the efficient alkoxycarbonylation of C−H bonds (Scheme 1, eq 2).[3] For example, Zhang developed a rhodium-catalyzed alkoxycarbonylation of sp^2 C−H bonds with CO toward esters.[4] In 2012, Huang described a Pd-catalyzed alkoxycarbonylation of sp^3 C−H bonds with CO.[5] Other significant achievements in alkoxycarbonylation of C−H bonds by carbamoyl chlorides,[6] oxaziridine,[7] and diethyl azodicarboxylate are well-documented.[8]

Scheme 1. Alkoxycarbonylation of ArX or ArH



Radical chemistry has attracted much attention in organic synthesis in the past decades.[9] However, the radical process for the preparation of esters is less developed.[10] Yu reported the Pd-catalyzed oxidative ethoxycarbonylation of the aromatic C−H bond with diethyl azodicarboxylate by ethoxyacyl radicals.[8] Carbazate was also applied to the construction of esters by alkoxycarbonyl radicals.[11] A sequential radical pathway is synthetically very promising since it could furnish short synthetic steps to access heterocycles.[12] Recently, isocyanides were developed to form 6-substituted phenanthridines that are abundant in natural products and pharmaceuticals,[13] proceeding through the addition of a radical to the isonitrile to form an imidolyl radical, followed by intramolecular cyclization. For example, 6-arylation,[14] 6-trifluoromethylation,[15] 6-phosphorylation,[16] 6-acylation,[17] and 6-alkylation[18] of 2-isocyanobiphenyl with different radical precursors were developed. Herein we report an oxidative alkoxycarbonylation of 2-isocyanobiphenyl with carbazates to provide phenanthridine-6-carboxylates by sequential radical addition−cyclization reactions (Scheme 1, eq 3).

Initially, the reaction of 2-isocyanobiphenyl (**1a**) with methyl carbazate (**2a**) in the presence of the radical initiator *tert*-butyl hydroperoxide (TBHP) with $FeCl_2$ as the catalyst was examined. To our delight, the desired methyl phenanthridine-6-carboxylate (**3aa**) was obtained in 51% yield (Table 1, entry 1). After screening of a series of catalysts, such as $FeCl_2$, $Fe(acac)_2$, $FeCl_3$, and CuI, $Fe(acac)_2$ was found to be the most efficient (Table 1, entry 2). Subsequently, we attempted to

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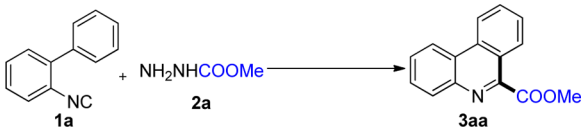
Table 1. Optimization of the Reaction Conditions[a]



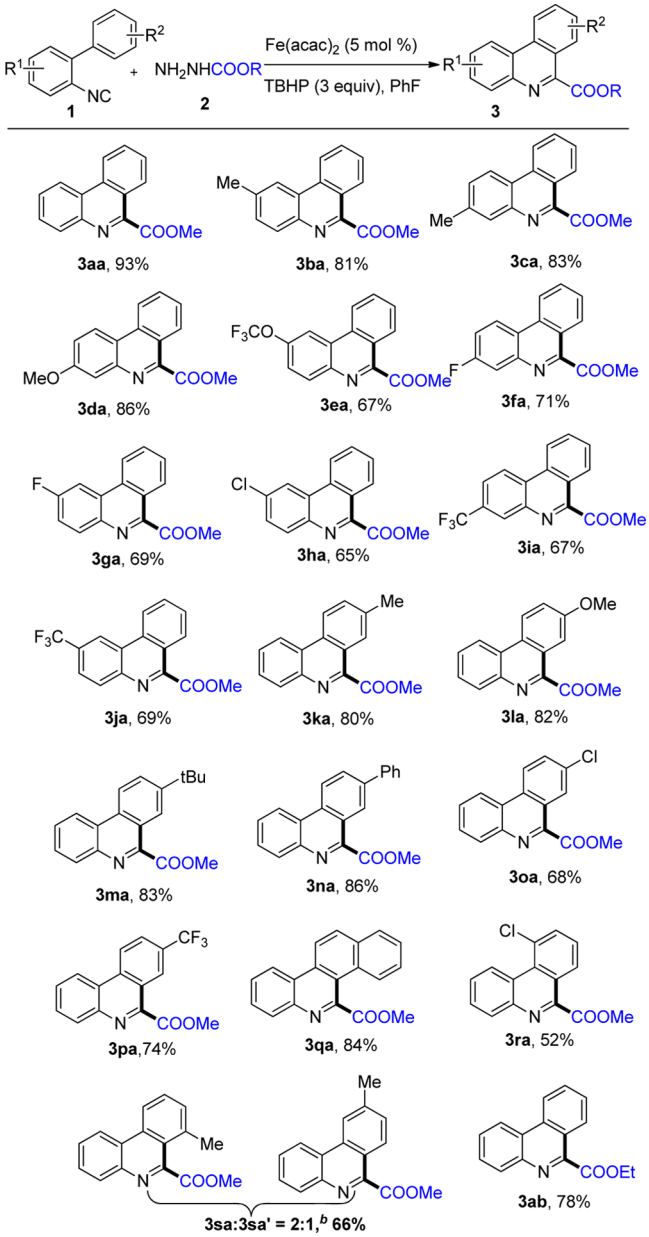
entry	[M]	radical initiator	solvent	yield (%)
1	$FeCl_2$	TBHP	CH_3CN	51
2	$Fe(acac)_2$	TBHP	CH_3CN	76
3	$FeCl_3$	TBHP	CH_3CN	37
4	CuI	TBHP	CH_3CN	32
5	$Fe(acac)_2$	DTBP	CH_3CN	26
6	$Fe(acac)_2$	BPO	CH_3CN	33
7	$Fe(acac)_2$	DCP	CH_3CN	8
8	$Fe(acac)_2$	TBHP	DCE	83
9	$Fe(acac)_2$	TBHP	PhF	93
10	$Fe(acac)_2$	TBHP	$PhCF_3$	77
11	$Fe(acac)_2$	TBHP	benzene	70
12	$Fe(acac)_2$	TBHP	PhCl	75
13	none	TBHP	PhF	33

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), [M] (5 mol %), radical initiator (0.6 mmol), and solvent (1.5 mL) under a N_2 atmosphere for 12 h at 80 °C. TBHP was used as a 70% solution in water. DTBP = di-*tert*-butyl peroxide. BPO = benzoyl peroxide. DCP = dicumyl peroxide.

promote the yield by surveying solvents such as DCE, PhF, $PhCF_3$, PhCl, and benzene. Among the solvents screened, PhF was the best, providing **3aa** in 93% yield (Table 1, entry 9). Using DTBP, BPO, or DCP instead of TBHP resulted in low yields (Table 1, entries 5−7). The control experiment demonstrated that the radical reaction could also occur without catalyst but gave an unsatisfying result (Table 1, entry 13). Consequently, the optimum reaction conditions were determined to be $Fe(acac)_2$ (5 mol %) and TBHP (3 equiv) in PhF at 80 °C under N_2 (Table 1, entry 9).

To explore the substrate scope of this protocol, the optimized reaction conditions were applied to a series of 2-isocyanobiaryl compounds. As shown in Table 2, various functional groups such as methoxy, chloro, fluoro, trifluoromethoxy, and trifluoromethyl groups were tolerated well under the present oxidative conditions, affording the products in good yields. We studied the effect of the substituents on the aromatic ring with the isocyanide group. As expected, the corresponding phenanthridine-6-carboxylates were obtained in good yields. Aromatic rings possessing electron-donating groups (**1b−d**; Table 2) gave higher yields than those with electron-withdrawing groups (**1f−j**; Table 2). Subsequently, the effects of substituents at the 4-position of the aromatic ring without the isocyanide group were investigated. The isocyanides **1k−m** bearing electron-donating groups provided the corresponding products in higher yields than did the electron-withdrawing analogues **1o** and **1p**. Notably, halogen groups were tolerable, which was suitable for potential further functionalization. 2-Isocyanobiphenyl bearing an *ortho* substituent revealed a lower reactivity due to the steric effect (Table 2, **3ra**). To investigate the regioselectivity of the cyclization, 2-isocyanobiphenyl **1s** bearing a *m*-methyl group was investigated, and it afforded a mixture of two regioisomers in a 2:1 ratio (Table 2, **3sa** + **3sa′**). As expected, when ethyl carbazate **2b** as an ethoxycarbonyl surrogate was employed, the arylethoxycarbonylation also ran well to afford ethyl phenanthridine-6-carboxylate (**3ab**) in good yield.

Table 2. Substrate Scope[a]



[a]Reaction conditions: **1** (0.2 mmol), **2** (0.4 mmol), $Fe(acac)_2$ (5 mol %), TBHP (0.6 mmol, 70% solution in water), and PhF (1.5 mL) under a N_2 atmosphere for 12 h at 80 °C. [b]The ratio of isomers was determined by ^1H NMR analysis of the isolated products.

To have a better understanding of the difunctionalization of 2-isocyanobiphenyl, some mechanistic experiments were carried out. A 1:1 mixture of substrates **1a** and **1a′** was used to determine the intermolecular kinetic isotope effect, and no kinetic isotope effect (k_H/k_D = 1) was observed (Scheme 2, eq 1). This result revealed that the arylation step may be compatible with either the S_EAr mechanism or the free radical mechanism.[19] When 2.0 equiv of 2,2,6,6-tetramethylpiperidine oxide (TEMPO) was added as a radical inhibitor, the desired product was not observed and the TEMPO−COOMe adduct was detected by ESI (Scheme 2, eq 2), providing evidence favoring the free radical mechanism.

On the basis of the above experimental results, a possible mechanism is proposed in Scheme 3. Initially, Fe(II)-assisted

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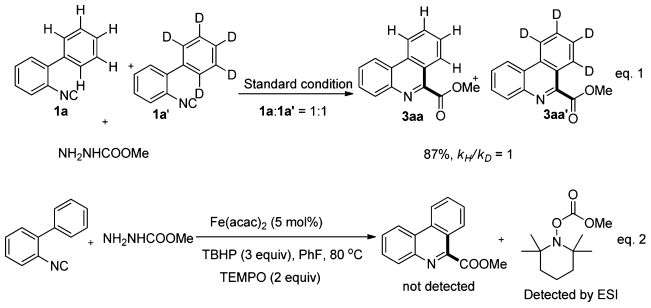
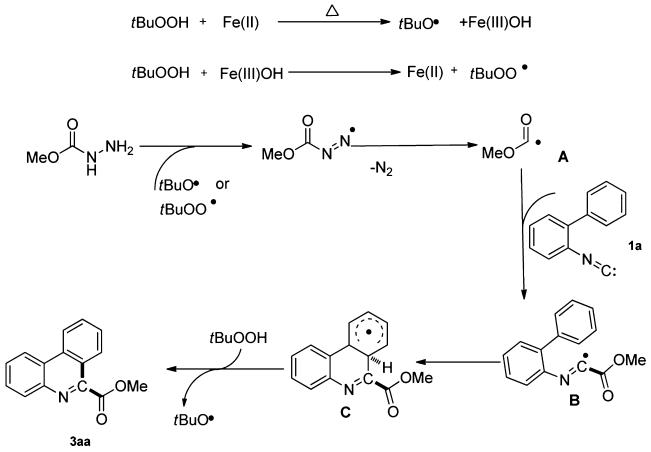
Scheme 2. Preliminary Mechanistic Study



Scheme 3. Proposed Mechanism



homolysis of TBHP into *tert*-butoxy radical and *tert*-butylperoxy radical occurs. With the aid of Fe(II), the homolysis of TBHP into *tert*-butoxy radical may be accelerated by single-electron transfer along with the formation of an Fe(III) species.[20] Then, C−N bond cleavage of the carbazate forms alkoxycarbonyl radical **A** with the release of N_2 through stepwise hydrogen abstraction.[11] Then radical **A** attacks the N═C bond of 2-isocyanobiaryl **1a** to form imidoyl radical **B**, which upon intramolecular cyclization with an aryl ring gives radical intermediate **C**. Finally, hydrogen abstraction of radical intermediate **C** takes place, providing the desired product **3aa**.

In summary, we have developed a novel sequential radical bimolecular C−C coupling of 2-isocyanobiaryls with carbazates to provide phenanthridine-6-carboxylates. As the oxidant for this procedure, cheap and commercially available TBHP is used. The procedure involves dual C−C bond formation by sequential radical addition and cyclization reactions.

EXPERIMENTAL SECTION

General Information. NMR spectra were measured on 400 MHz NMR spectrometers (400 MHz for ^{1}H, 100 MHz for ^{13}C, 376 MHz for ^{19}F) using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard. Chemical shifts (δ) are given in parts per million relative to TMS, and coupling constants (J) are given in hertz. ^{13}C NMR spectra were recorded at 100 MHz with complete proton decoupling. HRMS was performed on a TOF LC/MS equipped with an ESI probe operating in positive or negative ion mode. 2-Isocyanobiaryl compounds were prepared according to the reported procedure.[14a]

General Procedure for the Sequential Radical Coupling of 2-Isocyanobiaryls with $NH_2NHCOOMe$. A mixture of 2-isocyanobiaryl **1** (0.2 mmol), $NH_2NHCOOMe$ (**2a**) (0.4 mmol, 36 mg), $Fe(acac)_2$ (5 mol %, 2.5 mg), TBHP (0.6 mmol, 70% solution in H_2O), and PhF (1.5 mL) was added to a sealed tube. The sealed tube was evacuated and back-filled with N_2. The reaction mixture was vigorously stirred at 80 °C for 12 h. After the completion of the reaction, the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography or preparative TLC on GF254 (petroleum/ethyl acetate) to afford the desired product **3**.

*Methyl Phenanthridine-6-carboxylate (**3aa**).*[21] White solid (44 mg, 93%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.64−8.61 (m, 2H), 8.56 (d, J = 8.3 Hz, 1H), 8.28 (d, J = 7.8 Hz, 1H), 7.86 (d, J = 8.3 Hz, 1H), 7.79−7.69 (m, 3H), 4.12 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.5, 150.3, 142.6, 133.4, 131.1, 130.9, 129.0, 128.7, 127.9, 127.3, 124.9, 123.5, 122.1, 122.0, 53.2.

*Methyl 2-Methylphenanthridine-6-carboxylate (**3ba**).* Green solid (40.6 mg, 81%), mp 162−164 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.64 (d, J = 8.4 Hz, 2H), 8.61 (d, J = 8.4 Hz, 1H), 8.33 (s, 1H), 8.18 (d, J = 8.4 Hz, 1H), 7.84 (t, J = 8.2 Hz, 1H), 7.70 (t, J = 8.1 Hz, 1H), 7.60−7.57 (m, 1H), 4.14 (s, 3H), 2.62 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.5, 149.1, 140.7, 139.1, 133.1, 131.1, 130.9, 130.5, 127.8, 127.4, 124.9, 123.6, 122.1, 121.6, 53.2, 22.2. HRMS (ESI) m/z: calcd for $C_{16}H_{13}NNaO_2$ $[M + Na]^+$ 274.0838, found 274.0840.

*Methyl 3-Methylphenanthridine-6-carboxylate (**3ca**).* White solid (41.6 mg, 83%), mp 81−83 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.61−8.56 (m, 2H), 8.42 (d, J = 8.4 Hz, 1H), 8.06 (s, 1H), 7.83 (t, J = 8.3 Hz, 1H), 7.67 (t, J = 8.3 Hz, 1H), 7.53 (d, J = 8.4 Hz, 1H), 4.14 (s, 3H), 2.57 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.6, 150.2, 142.7, 139.3, 133.5, 131.1, 130.5, 130.4, 127.5, 127.3, 123.2, 122.6, 121.9, 121.8, 53.2, 21.5. HRMS (ESI) m/z: calcd for $C_{16}H_{13}NNaO_2$ $[M + Na]^+$ 274.0838, found 274.0839.

*Methyl 3-Methoxyphenanthridine-6-carboxylate (**3da**).* Yellowish solid (45.9 mg, 86%), mp 110−112 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.60 (d, J = 8.3 Hz, 1H), 8.52 (d, J = 8.4 Hz, 1H), 8.45−8.42 (m, 1H), 7.81 (t, J = 8.1 Hz, 1H), 7.67−7.62 (m, 2H), 7.37−7.34 (m, 1H), 4.15 (s, 3H), 3.97 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.5, 160.3, 150.5, 144.2, 133.7, 131.2, 127.4, 126.9, 123.2, 122.7, 121.6, 120.3, 119.1, 110.2, 55.7, 53.3. HRMS (ESI) m/z: calcd for $C_{16}H_{13}NNaO_3$ $[M + Na]^+$ 290.0788, found 290.0787.

*Methyl 2-(Trifluoromethoxy)phenanthridine-6-carboxylate (**3ea**).* Brown liquid (43 mg, 67%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.65 (d, J = 8.0 Hz, 1H), 8.57 (d, J = 8.3 Hz, 1H), 8.37 (s, 1H), 8.32 (d, J = 9.0 Hz, 1H), 7.92 (t, J = 8.3 Hz, 1H), 7.78 (d, J = 8.2 Hz, 1H), 7.63 (d, J = 8.2 Hz, 1H), 4.15 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.2, 150.8, 148.96, 148.94, 140.8, 133.0, 132.8, 131.6, 128.8, 127.6, 126.0, 123.6, 122.4, 122.2, 113.5, 53.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ −57.5. HRMS (ESI) m/z: calcd for $C_{16}H_{10}F_3NNaO_3$ $[M + Na]^+$ 344.0505, found 344.0503.

*Methyl 3-Fluorophenanthridine-6-carboxylate (**3fa**).* Yellowish solid (36.2 mg, 71%), mp 128−130 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.57−8.50 (m, 3H), 7.93−7.90 (m, 1H), 7.86 (t, J = 8.2 Hz, 1H), 7.70 (t, J = 8.1 Hz, 1H), 7.50−7.45 (m, 1H), 4.15 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.3, 162.7 (d, J_{C-F} = 247.8 Hz), 151.7, 143.8 (d, J_{C-F} = 11.9 Hz), 133.2, 131.6, 127.8, 127.5, 124.1 (d, J_{C-F} = 9.4 Hz), 123.0, 121.9, 121.6, 117.9 (d, J_{C-F} = 23.8 Hz), 115.2 (d, J_{C-F} = 20.6 Hz), 53.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ −110.9. HRMS (ESI) m/z: calcd for $C_{15}H_{10}FNNaO_2$ $[M + Na]^+$ 278.0588, found 278.0586.

*Methyl 2-Fluorophenanthridine-6-carboxylate (**3ga**).* Yellowish solid (35.2 mg, 69%), mp 144−146 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.66 (d, J = 8.2 Hz, 1H), 8.50 (d, J = 8.3 Hz, 1H), 8.29−8.25 (m, 1H), 8.17−8.14 (m, 1H), 7.87 (d, J = 8.3 Hz, 1H), 7.75 (d, J = 8.3 Hz, 1H), 7.53−7.48 (m, 1H), 4.15 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.3, 162.8 (d, J_{C-F} = 248.6 Hz), 149.4 (d, J_{C-F} = 2.9 Hz), 139.4 (d, J_{C-F} = 1.3 Hz), 133.3 (d, J_{C-F} = 9.4 Hz), 132.8 (d, J_{C-F} = 4.3 Hz), 131.2, 128.6, 127.5, 126.6 (d, J_{C-F} = 9.4 Hz), 123.5, 122.3, 118.2 (d, J_{C-F} = 24.4 Hz), 107.1 (d, J_{C-F} = 23.4 Hz), 53.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ −109.4. HRMS (ESI) m/z: calcd for $C_{15}H_{10}FNNaO_2$ $[M + Na]^+$ 278.0588, found 278.0589.

*Methyl 2-Chlorophenanthridine-6-carboxylate (**3ha**).* White solid (35.2 mg, 65%), mp 132−133 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.62 (d, J = 8.3 Hz, 1H), 8.52 (d, J = 8.3 Hz, 1H), 8.50 (s, 1H), 8.19

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(d, J = 8.8 Hz, 1H), 7.87 (t, J = 8.3 Hz, 1H), 7.74 (t, J = 8.2 Hz, 1H), 7.71−7.68 (m, 1H), 4.15 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.2, 150.4, 140.9, 134.9, 132.4, 132.3, 131.5, 129.7, 128.6, 127.5, 125.9, 123.7, 122.2, 121.8, 53.3. HRMS (ESI) m/z: calcd for $C_{15}H_{10}ClNNaO_2$ $[M + Na]^+$ 294.0292, found 294.0289.

*Methyl 3-(Trifluoromethyl)phenanthridine-6-carboxylate (**3ia**).* Semisolid (40.9 mg, 67%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.64−8.61 (m, 3H), 8.57 (s, 1H), 7.94−7.89 (m, 2H), 7.81−7.77 (m, 1H), 4.16 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.0, 151.7, 141.8, 132.6, 131.8, 130.9 (q, J_{C-F} = 32.9 Hz), 129.1, 128.4 (q, J_{C-F} = 4.1 Hz), 127.6, 127.1, 124.4 (q, J_{C-F} = 3.1 Hz), 124.0, 123.2, 122.5, 53.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ −62.4. HRMS (ESI) m/z: calcd for $C_{16}H_{10}F_3NNaO_2$ $[M + Na]^+$ 328.0556, found 328.0558.

*Methyl 2-(Trifluoromethyl)phenanthridine-6-carboxylate (**3ja**).* White solid (42 mg, 69%), mp 112−114 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.73 (s, 1H), 8.54 (d, J = 8.3 Hz, 1H), 8.49 (d, J = 8.3 Hz, 1H), 8.27 (d, J = 8.5 Hz, 1H), 7.88−7.81 (m, 2H), 7.70−7.66 (m, 1H), 4.07 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.1, 152.5, 143.9, 133.1, 131.9, 131.8, 130.2 (q, J_{C-F} = 32.7 Hz), 128.8, 127.6, 125.4, 125.0 (q, J_{C-F} = 3.1 Hz), 124.5, 123.6, 122.7, 122.1, 119.9 (q, J_{C-F} = 4.2 Hz), 53.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ −62.0. HRMS (ESI) m/z: calcd for $C_{16}H_{10}F_3NNaO_2$ $[M + Na]^+$ 328.0556, found 328.0555.

*Methyl 8-Methylphenanthridine-6-carboxylate (**3ka**).* White solid (40.2 mg, 80%), mp 80−81 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.53−8.50 (m, 2H), 8.36 (s, 1H), 8.27−8.25 (m, 1H), 7.75−7.66 (m, 3H), 4.15 (s, 3H), 2.58 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.6, 150.1, 142.2, 138.1, 133.0, 131.4, 130.8, 128.6, 126.6, 125.0, 123.6, 122.2, 121.9, 53.2, 21.9. HRMS (ESI) m/z: calcd for $C_{16}H_{13}NNaO_2$ $[M + Na]^+$ 274.0838, found 274.0840.

*Methyl 8-Methoxyphenanthridine-6-carboxylate (**3la**).* Yellow solid (43.6 mg, 82%), mp 203−205 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.56−8.54 (m, 1H), 8.50−8.48 (m, 1H), 8.28−8.25 (m, 1H), 8.15 (s, 1H), 7.72−7.70 (m, 2H), 7.51−7.48 (m, 1H), 4.15 (s, 3H), 3.99 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.6, 159.1, 148.5, 141.8, 131.0, 128.9, 128.1, 125.3, 125.2, 123.7, 122.5, 121.6, 106.7, 55.6, 53.2. HRMS (ESI) m/z: calcd for $C_{16}H_{13}NNaO_3$ $[M + Na]^+$ 290.0788, found 290.0786.

*Methyl 8-(tert-Butyl)phenanthridine-6-carboxylate (**3ma**).* Brown liquid (48.6 mg, 83%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.65−8.64 (m, 1H), 8.59−8.53 (m, 2H), 8.29−8.26 (m, 1H), 7.97−7.95 (m, 1H), 7.76−7.69 (m, 2H), 4.16 (s, 3H), 1.46 (s, 9H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.7, 151.1, 150.2, 142.4, 131.4, 130.9, 129.7, 128.7, 125.0, 123.6, 122.8, 122.0, 121.9, 53.2, 35.2, 31.2. HRMS (ESI) m/z: calcd for $C_{19}H_{19}NNaO_2$ $[M + Na]^+$ 316.1308, found 316.1305.

*Methyl 8-Phenylphenanthridine-6-carboxylate (**3na**).* Yellowish solid (53.8 mg, 86%), mp 136−138 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.86 (s, 1H), 8.67 (d, J = 8.6 Hz, 1H), 8.56 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 7.4 Hz, 1H), 8.10 (d, J = 8.6 Hz, 1H), 7.77−7.73 (m, 4H), 7.51 (t, J = 7.4 Hz, 2H), 7.41 (t, J = 7.3 Hz, 1H), 4.16 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.5, 150.2, 142.5, 140.7, 140.0, 132.4, 131.0, 130.5, 129.0, 128.9, 128.0, 127.5, 125.3, 124.8, 124.0, 122.8, 122.1, 53.3. HRMS (ESI) m/z: calcd for $C_{21}H_{15}NNaO_2$ $[M + Na]^+$ 336.0995, found 336.0994.

*Methyl 8-Chlorophenanthridine-6-carboxylate (**3oa**).* White solid (36.8 mg, 68%), mp 126−128 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.81 (d, J = 8.3 Hz, 1H), 8.51 (d, J = 8.3 Hz, 1H), 8.49 (s, 1H), 8.20 (d, J = 8.8 Hz, 1H), 7.87 (d, J = 8.3 Hz, 1H), 7.74 (d, J = 8.3 Hz, 1H), 7.41−7.68 (m, 1H), 4.15 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.5, 150.3, 140.7, 134.9, 132.4, 132.2, 131.6, 129.8, 128.6, 127.5, 125.9, 123.6, 122.1, 121.7, 53.3. HRMS (ESI) m/z: calcd for $C_{15}H_{10}ClNNaO_2$ $[M + Na]^+$ 294.0292, found 294.0290.

*Methyl 8-(Trifluoromethyl)phenanthridine-6-carboxylate (**3pa**).* Yellowish solid (45 mg, 74%), mp 90−92 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.04 (s, 1H), 8.69 (d, J = 8.7 Hz, 1H), 8.54 (d, J = 8.0 Hz, 1H), 8.30 (d, J = 8.0 Hz, 1H), 8.03 (d, J = 8.7 Hz, 1H), 7.86−7.76 (m, 2H), 4.17 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 165.9, 149.4, 143.1, 135.4, 131.2, 130.2, 129.7 (q, J_{C-F} = 32.7 Hz), 129.4, 126.9 (q, J_{C-F} = 3.1 Hz), 125.2 (q, J_{C-F} = 4.5 Hz), 124.0, 123.2, 122.9, 122.5, 122.4, 53.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ −62.3. HRMS (ESI) m/z: calcd for $C_{16}H_{10}F_3NNaO_2$ $[M + Na]^+$ 328.0556, found 328.0556.

*Methyl Benzo[i]phenanthridine-5-carboxylate (**3qa**).* Colorless liquid (48.2 mg, 84%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.51 (d, J = 8.3 Hz, 1H), 8.46 (d, J = 9.0 Hz, 1H), 8.31 (d, J = 8.3 Hz, 1H), 8.26 (d, J = 8.3 Hz, 1H), 8.05 (d, J = 9.0 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.75 (t, J = 8.2 Hz, 1H), 7.69−7.58 (m, 3H), 4.14 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 169.9, 150.4, 143.3, 133.9, 132.8, 132.6, 130.1, 129.4, 129.1, 128.5, 128.1, 127.6, 127.1, 124.7, 124.4, 122.6, 119.7, 119.0, 53.4. HRMS (ESI) m/z: calcd for $C_{19}H_{13}NNaO_2$ $[M + Na]^+$ 310.0838, found 310.0837.

*Methyl 10-Chlorophenanthridine-6-carboxylate (**3ra**).* White solid (28.1 mg, 52%), mp 109−111 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.83 (d, J = 8.6 Hz, 1H), 8.47 (d, J = 8.2 Hz, 1H), 8.31 (d, J = 8.0 Hz, 1H), 7.96 (d, J = 7.7 Hz, 1H), 7.87−7.82 (m, 1H), 7.79−7.75 (m, 1H), 7.63 (d, J = 8.0 Hz, 1H), 4.16 (s, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.6, 151.1, 143.7, 135.0, 131.5, 131.0, 130.3, 129.5, 128.2, 127.7, 126.7, 126.4, 125.7, 123.9, 53.4. HRMS (ESI) m/z: calcd for $C_{15}H_{10}ClNNaO_2$ $[M + Na]^+$ 294.0292, found 294.0294.

*Methyl 7-Methylphenanthridine-6-carboxylate (**3sa**) and Methyl 9-Methylphenanthridine-6-carboxylate (**3sa′**).* Brown liquid (33 mg, 66%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.55−8.51 (m, 3H), 8.41 (s, 0.51H), 8.26 (d, J = 8.3 Hz, 0.5H), 8.19 (d, J = 8.3 Hz, 1H), 7.77−7.66 (m, 4H), 7.53 (d, J = 8.5 Hz, 0.59H), 7.49 (d, J = 7.2 Hz, 1.12H), 4.24 (s, 1.45H), 4.11 (s, 2.9H), 2.72 (s, 3H), 2.63 (s, 1.5H). HRMS (ESI) m/z: calcd for $C_{16}H_{13}NNaO_2$ $[M + Na]^+$ 274.0838, found 274.0837.

Ethyl Phenanthridine-6-carboxylate (3ab).[21] Compound **3ab** was obtained using **1a** and $NH_2NHCOOEt$ (**2b**). White solid (39.1 mg, 78%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.63 (d, J = 8.3 Hz, 1H), 8.57−8.52 (m, 2H), 8.29 (d, J = 7.8 Hz, 1H), 7.86 (t, J = 8.2 Hz, 1H), 7.78−7.69 (m, 3H), 4.64 (q, J = 7.2 Hz, 2H), 1.53 (t, J = 7.2 Hz, 3H). ^{13}C NMR {1H} ($CDCl_3$, 100 MHz): δ 166.2, 151.0, 142.4, 133.4, 131.3, 130.7, 129.1, 128.6, 127.9, 127.3, 124.8, 123.3, 122.2, 122.0, 62.5, 14.4.

Intermolecular Competition Experiment with Isotopically Labeled 1a′. A mixture of 2-isocyanobiaryl **1a** (0.1 mmol) and the labeled analogue **1a′** (0.1 mmol), $NH_2NHCOOMe$ **2a** (0.4 mmol), $Fe(acac)_2$ (5 mol %, 2.5 mg), TBHP (0.6 mmol, 70% in H_2O), and PhF (1.5 mL) was added to a sealed tube, which was evacuated and back-filled with N_2. The reaction mixture was vigorously stirred at 80 °C for 12 h. After the completion of the reaction, the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel or preparative TLC on GF254 to afford the desired products **3aa** and **3aa′**. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.67−8.62 (m, 1H), 8.59 (d, J = 7.7 Hz, 1H), 7.88 (d, J = 8.2 Hz, 0.51H), 7.80−7.71 (m, 2.52H), 4.15 (s, 3H).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra of compounds **3aa**−**sa** and **3ab** and ^{19}F NMR spectra of compounds **3ea**, **3fa**, **3ga**, **3ia**, **3ja**, and **3pa**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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